3. Remarks

Claims 17-26 and 31-36, are pending in the application with claims 19 and 20 being in independent format. Claims 19 and 20 have been amended to delete claims to fragments of variants. Applicants kindly request reconsideration and allowance of the claims.

35 U.S.C. §112

Claims 17-26 and 31-36 stand rejected under 35 U.S.C. §112, first paragraph for lack of enablement.

Applicant's interview with the Examiner on October 19, 2004 clarified some of the objective criteria required of Applicant's disclosure in order to support variant language in the claims. Applicants reemphasize that the present application is unique in its *substantive* description of the Flt3-L protein that satisfy those criteria. Applicants have an exceptionally strong case in favor of 90% variant language due to the fact that Applicants were the first to discover and fully disclose:

1. The cDNA and polypeptide sequences for *two* species: human (SEQ ID NO:6) and mouse (SEQ ID NO:2). See Examples 3 and 4. Applicants note that the U.S.P.T.O.'s written description guidelines (Example 14: Product by Function) only requires *one* species be disclosed to support variant language.
2. Functional domains for each orthologue. For the human protein: extracellular (amino acids 28-182 of SEQ ID NO:6), transmembrane (amino acids 183-205 of SEQ ID NO:6), intracellular domain (amino acids 206-235 of SEQ ID NO:6), and signal sequence (amino acids 1-27 of SEQ ID NO:6). See Example 4 at page 34 and SEQ ID NO:6 for the human protein and Example 3 at page 29 for the mouse.
3. Flt3-L biological activity, *i.e.*, binding the flt3 receptor and stimulating the proliferation of stem and progenitor cells.
4. Fragments of the extracellular domain that retain the ability to bind the flt3 receptor and stimulate hematopoiesis (amino acids 28-160 of SEQ ID NO:6 is a biologically active fragment of the extracellular domain, which spans amino acids 28-182 of SEQ ID NO:6). See page 12, lines 12-15.

Applicants note that there is about 72% identity between the mouse and human orthologues (see page 34, line 32) and both orthologues share the same biological activity – binding their respective flt3 receptors and stimulating the proliferation of stem and progenitor cells. Thus, 72% identity legitimately defines the genus, and yet, Applicants are only seeking 90% variants.

In addition, search results for the claimed sequence show that the identity of the closest protein is only between 27-45% (see attached BLAST results). Clearly, the percent variants encompassed by the claims do not read on anything but human Flt3-L.

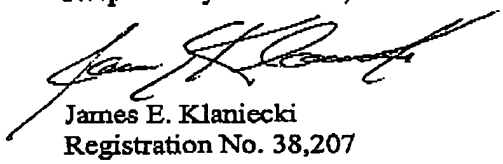
It is important to remember that the claims are limited by the requirement that all Flt3-L proteins must bind the flt3 receptor, which is a stringent limitation on the actual number of variants encompassed by the claims. Applicants respectfully remind the Examiner that variant language is permissible under the U.S.P.T.O.'s written description guidelines (Example 14: Product by Function) and that Applicants' disclosure far exceeds the scenario described in Example 14.

As to the enablement issue, Applicants' disclosure fully meets the requirement that the specification teach one of skill in the art to make and use the invention. With regard to variants, Applicants' specification teaches procedures for making biologically active variants at page 8, line 5, *et seq.*; teach oligonucleotide-directed site-specific mutagenesis procedures may be used to create variants (page 13, line 27, *et seq.*); assays are described for identifying variants that bind the flt3 receptor (page 16, line 26 to page 19, line 2, as well as Examples 10 and 11 for biological function assays).

Applicants note that procedures for making variants and assaying for binding to a soluble receptor were quite routine and conventional in the art at the time the application was filed. Consequently, no undue experimentation would be required.

Applicants respectfully request the rejection under 35 U.S.C. §112 be properly withdrawn. Reconsideration and allowance of the pending claims is kindly requested.

Respectfully submitted,



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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this correspondence is being facsimile transmitted to the United States Patent and Trademark Office on the date indicated below.

Signed: Nanci M. Kertson Date: October 21, 2004

Nanci M. Kertson